

Appln. No. 09/806,636

AMENDMENT AFTER FINAL REJECTION UNDER 37 CFR 1.116

AND SUMMARY OF TELEPHONIC AND PERSONAL INTERVIEWS

Docket No. FJIN-109

**Amendment to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

Please cancel Claims 1 and 27, without prejudice to or disclaimer of the subject matter therein, and amend Claims 2, 4, 6, 8-24, and 30 as follows:

**Listing of Claims:**

1. (Canceled)
2. (Currently Amended) The controlled-release oral preparation of esculetin according to claim [[1]] 28, containing 0.5 to 90 wt % of the gel-forming polymer base.
3. (Original) The controlled-release oral preparation of esculetin according to claim 2, wherein the gel-forming polymer base is hydroxypropylmethylcellulose.
4. (Currently Amended) The controlled-release oral preparation of esculetin according to claim [[1]] 30, containing 0.5 to 50 wt % of an enteric coating base.
5. (Previously presented) The controlled-release oral preparation of esculetin according to claim 4, wherein the enteric coating base is selected from the group consisting of hydroxypropylmethylcellulose acetate succinate, hydroxypropylmethylcellulose phthalate, cellulose acetate phthalate, carboxymethylethylcellulose, and methacrylic acid copolymer.

6. (Currently Amended) The controlled-release oral preparation of esculetin according to claim ~~[[1]]~~ 28, containing 0.5 to 50 wt % of an insoluble coating base.

7. (Previously presented) The controlled-release oral preparation of esculetin according to claim 6, wherein the insoluble coating base is ethylcellulose.

8. (Currently Amended) The controlled-release oral preparation of esculetin according to claim ~~[[6]]~~ 30, comprising 0.5 to 90 wt % of ~~[[a]]~~ the gel-forming polymer base, and 0.5 to 50 wt % of ~~[[an]]~~ the enteric coating base ~~[[and/or]]~~ and 0.5 to 50 wt % of an insoluble coating base.

9. (Currently Amended) The controlled-release oral preparation of esculetin according to claim ~~[[1]]~~ 28, ~~of which~~ wherein the release of esculetin or its derivative is controlled so that the concentration of glucuronic acid conjugates in plasma is maintained at 0.5  $\mu\text{mol/L}$  or more for a period of 10 hours or more after administration when the ~~preparation is orally administered to a beagle dog at a dose of 1-100 mg/kg.~~

10. (Currently Amended) The controlled-release oral preparation of esculetin according to claim ~~[[1]]~~ 28, ~~of which~~ wherein the release of esculetin is controlled so that the period of time required for the preparation to dissolve 80 wt % of esculetin is 0.5 to 23 hours as determined by the dissolution test according to the paddle method of the Japanese Pharmacopoeia.

11. (Currently Amended) The controlled-release oral preparation of esculetin according to claim 2, ~~of which~~ wherein the release of esculetin or its derivative is controlled so that the concentration of glucuronic acid conjugates in plasma is maintained at 0.5  $\mu\text{mol/L}$  or more for a period of 10 hours or more after administration when the preparation is orally administered to a beagle dog at a dose of 1-100 mg/kg.

12. (Currently Amended) The controlled-release oral preparation of esculetin according to claim 3, ~~of which~~ wherein the release of esculetin or its derivative is controlled so that the concentration of glucuronic acid conjugates in plasma is maintained at 0.5  $\mu\text{mol/L}$  or more for a period of 10 hours or more after administration when the preparation is orally administered to a beagle dog at a dose of 1-100 mg/kg.

13. (Currently Amended) The controlled-release oral preparation of esculetin according to claim 4, ~~of which~~ wherein the release of esculetin or its derivative is controlled so that the concentration of glucuronic acid conjugates in plasma is maintained at 0.5  $\mu\text{mol/L}$  or more for a period of 10 hours or more after administration when the preparation is orally administered to a beagle dog at a dose of 1-100 mg/kg.

14. (Currently Amended) The controlled-release oral preparation of esculetin according to claim 5, ~~of which~~ wherein the release of esculetin or its derivative is controlled so that the concentration of glucuronic acid conjugates in plasma is maintained at 0.5  $\mu\text{mol/L}$  or more for a period of 10 hours or more after administration when the preparation is orally administered to a beagle dog at a dose of 1-100 mg/kg.

15. (Currently Amended) The controlled-release oral preparation of esculetin according to claim 6, ~~of which~~ wherein the release of esculetin or its derivative is controlled so that the concentration of glucuronic acid conjugates in plasma is maintained at 0.5  $\mu\text{mol/L}$  or more for a period of 10 hours or more after administration when the preparation is orally administered to a beagle dog at a dose of 1-100 mg/kg.

16. (Currently Amended) The controlled-release oral preparation of esculetin according to claim 7, ~~of which~~ wherein the release of esculetin or its derivative is controlled so that the concentration of glucuronic acid conjugates in plasma is maintained at 0.5  $\mu\text{mol/L}$  or more for a period of 10 hours or more after administration when the preparation is orally administered to a beagle dog at a dose of 1-100 mg/kg.

17. (Currently Amended) The controlled-release oral preparation of esculetin according to claim 8, ~~of which~~ wherein the release of esculetin or its derivative is controlled so that the concentration of glucuronic acid conjugates in plasma is maintained at 0.5  $\mu\text{mol/L}$  or more for a period of 10 hours or more after administration when the preparation is orally administered to a beagle dog at a dose of 1-100 mg/kg.

18. (Currently Amended) The controlled-release oral preparation of esculetin according to claim 2, ~~of which~~ wherein the release of esculetin is controlled so that the period of time required for the preparation to dissolve 80 wt % of esculetin is 0.5 to 23 hours as determined by the dissolution test according to the paddle method of the Japanese Pharmacopoeia.

Appln. No. 09/806,636

AMENDMENT AFTER FINAL REJECTION UNDER 37 CFR 1.116

AND SUMMARY OF TELEPHONIC AND PERSONAL INTERVIEWS

Docket No. FJIN-109

19. (Currently Amended) The controlled-release oral preparation of esculetin according to claim 3, ~~of which~~ wherein the release of esculetin is controlled so that the period of time required for the preparation to dissolve 80 wt % of esculetin is 0.5 to 23 hours as determined by the dissolution test according to the paddle method of the Japanese Pharmacopoeia.

20. (Currently Amended) The controlled-release oral preparation of esculetin according to claim 4, ~~of which~~ wherein the release of esculetin is controlled so that the period of time required for the preparation to dissolve 80 wt % of esculetin is 0.5 to 23 hours as determined by the dissolution test according to the paddle method of the Japanese Pharmacopoeia.

21. (Currently Amended) The controlled-release oral preparation of esculetin according to claim 5, ~~of which~~ wherein the release of esculetin is controlled so that the period of time required for the preparation to dissolve 80 wt % of esculetin is 0.5 to 23 hours as determined by the dissolution test according to the paddle method of the Japanese Pharmacopoeia.

22. (Currently Amended) The controlled-release oral preparation of esculetin according to claim 6, ~~of which~~ wherein the release of esculetin is controlled so that the period of time required for the preparation to dissolve 80 wt % of esculetin is 0.5 to 23 hours as determined by the dissolution test according to the paddle method of the Japanese Pharmacopoeia.

23. (Currently Amended) The controlled-release oral preparation of esculetin according to claim 7, ~~of which~~ wherein the release of esculetin is controlled so that the period of time required for the preparation to dissolve 80 wt % of esculetin is 0.5 to 23 hours as determined by the dissolution test according to the paddle method of the Japanese Pharmacopoeia.

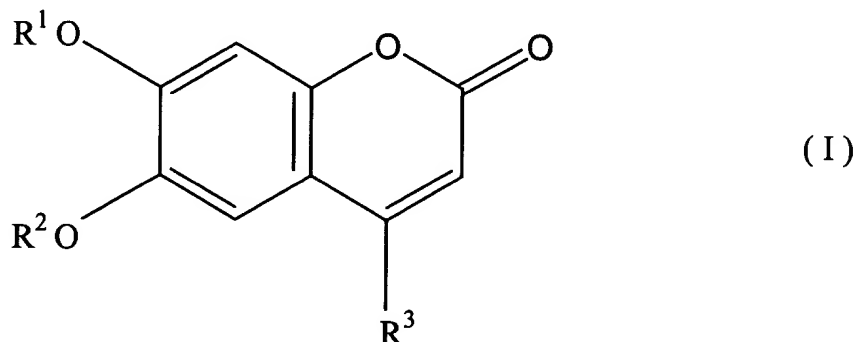
24. (Currently Amended) The controlled-release oral preparation of esculetin according to claim 8, ~~of which~~ wherein the release of esculetin is controlled so that the period of time required for the preparation to dissolve 80 wt % of esculetin is 0.5 to 23 hours as determined by the dissolution test according to the paddle method of the Japanese Pharmacopoeia.

25. (Previously presented) The controlled-release oral preparation according to claim 6, wherein the insoluble coating base is an aminoalkylmethacrylate copolymer.

26. (Previously presented) The controlled-release oral preparation of esculetin according to claim 8, wherein the enteric coating base is selected from the group consisting of hydroxypropylmethylcellulose acetate succinate, hydroxypropylmethylcellulose phthalate, cellulose acetate phthalate, carboxymethylethylcellulose, and methacrylic acid copolymer, and the insoluble coating base is selected from the group consisting of ethylcellulose and aminoalkylmethacrylate copolymer.

27. (Canceled)

28. (Previously presented) A controlled-release oral preparation comprising:  
a granulated mixture of: a) esculetin, or its derivative shown by the formula (I),

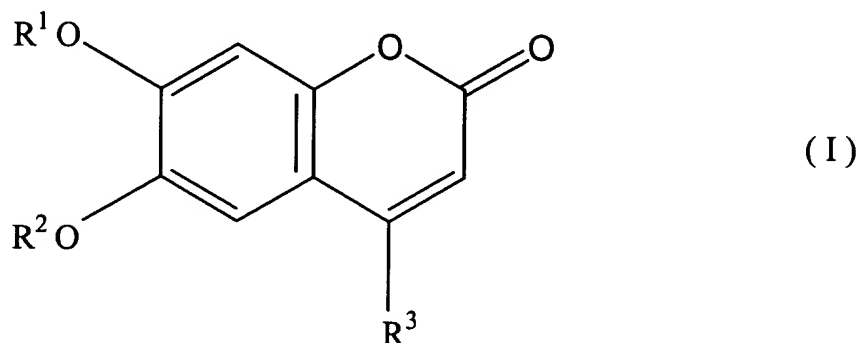


wherein R<sup>1</sup> and R<sup>2</sup> are individually a hydrogen atom or a saturated or unsaturated aliphatic acyl group having 2-25 carbon atoms or a benzoyl group, and R<sup>3</sup> is a hydrogen atom, hydroxyl group, alkyl group, aryl group, or aralkyl group, or a pharmaceutically acceptable salt thereof as an effective component; and b) a gel-forming polymer base; and an enteric capsule containing the granulated mixture.

~~29. (Previously presented) The controlled-release oral preparation of esculetin~~  
according to claim 28, wherein the enteric capsule comprises an enteric coating base selected from the group consisting of hydroxypropylmethylcellulose acetate succinate, hydroxypropylmethylcellulose phthalate, cellulose acetate phthalate, carboxymethylethylcellulose, and methacrylic acid copolymer.

30. (Currently Amended) A controlled-release oral preparation comprising  
consisting essentially of:

a tablet comprising a compressed mixture of: a) esculetin, or its derivative shown by the formula (I),



wherein R<sup>1</sup> and R<sup>2</sup> are individually a hydrogen atom or a saturated or unsaturated aliphatic acyl group having 2-25 carbon atoms or a benzoyl group, and R<sup>3</sup> is a hydrogen atom, hydroxyl group, alkyl group, aryl group, or aralkyl group, or a pharmaceutically acceptable salt thereof as an effective component; and b) a gel-forming polymer base; and an enteric coating base [[sprayed]] on the compressed mixture.

31. (Previously presented.) The controlled-release oral preparation of esculetin according to claim 30, wherein the enteric coating base is selected from the group consisting of hydroxypropylmethylcellulose acetate succinate, hydroxypropylmethylcellulose phthalate, cellulose acetate phthalate, carboxymethylethylcellulose, and methacrylic acid copolymer.